Amendments to the Specification

Please replace the paragraph starting at page 1, line 28, with the following paragraph:

--The invention is based, in part, on the discovery and identification of diabetes-mediating (DM) proteins. DM proteins are proteins which are involved in the development of diabetes or in the prevention of diabetes development in a subject at risk for the development of diabetes, and are identified by differential expression during the presence ~~and~~ or absence of disease development. The development of diabetes includes all stages which precede the clinically detectable stage.--

Please replace the paragraph starting at page 2, line 3, with the following paragraph:

--Accordingly, in one aspect the invention features substantially purified diabetes-mediating proteins exhibiting an altered expression during development of diabetes relative to expression in the absence of diabetes development. The purified diabetes-mediating proteins of the invention are selected from the proteins listed in Tables 1 and 2. Novel diabetes-mediating proteins are provided characterized by molecular weight, pI, and the mass spectroscopic characteristics as shown in FIGs. 6-40. These proteins, referred to by their position on 10% IEF (isoelectric focusing) or NEPHGE (non-equilibrium pH-gradient electrophoresis) 2-dimensional gels (FIGs. 1A-1B), are selected from the group consisting of NEPHGE 7, 9, 102, 123, 129, 130, 174, 181, 182, 211, 231, 236, 253, 298, and IEF 665, 939, 941, 950, 1196.--

Please replace the paragraph starting at page 4, line 8, with the following paragraph:

--The invention includes a substantially purified protective or deleterious diabetes-mediating protein, and polynucleotide sequence which encodes the diabetes-mediating protein of the invention. In one non-limiting embodiment, the protective protein is ~~galactin~~ galectin-3 (FIGs. 4 and 5) (SEQ ID NOs:1-2). In another non-limiting embodiment, the deleterious protein is mortalin (FIGs. 2-3) (SEQ ID NOs:3-4).--

Please replace the paragraph starting at page 4, line 21, with the following paragraph:

--In a related aspect, the invention features a transgenic mammal having an exogenous deleterious gene, and exhibiting an increased incidence of the spontaneous development of diabetes within a predictable period of time. In preferred embodiments, the transgenic mammal exhibits a greater than 50% chance, more preferably a greater than 60% chance, even more preferably a greater than 70% chance, even more preferably a greater than 80% chance, and most preferably a greater than 90% chance of developing diabetes. In an embodiment of the invention, the transgenic mammal of the invention is transgenic for one or more genes encoding a deleterious diabetes-mediating protein. In another embodiment, the transgenic mammal additionally has one or more endogenous diabetes-mediating protein genes ablated. Generally, the transgenic mammal will have the transgenic gene under control of an insulin, CMV (cytomegalovirus), interferon, or MHC (myosin heavy chain) promoter. In further specific embodiments, a transgenic mammal expresses elevated levels of an endogenous diabetes-mediating gene obtained by an enhanced promoter or a high copy number of an endogenous diabetes-mediating protein gene. In further specific embodiments, the transgenic mammal has a disrupted diabetes-mediating protein gene.--

Please replace the paragraph starting at page 5, line 15, with the following paragraph:

--In a related aspect, the invention provides or an assay for identifying a compound which modulates the activity of a diabetes-mediating protein, e.g., an agonist, an antagonist, or by blocking a post-translational step required for activation of a diabetes-mediating protein. Changes in the expression of specific DM proteins are useful in a screening method for identifying compounds capable of ~~modulate~~ modulating the expression of DM proteins. A compound which modulates the expression of one or more diabetes mediating proteins is useful as a potential therapeutic in the treatment or prevention of diabetes. Accordingly, in one aspect the invention features an assay method for identifying compounds capable of modulating the expression of diabetes-mediating proteins having the steps of contacting a test compound with a cell or tissue expressing one or more diabetes-mediating proteins, and determining the effect of the test compound on the expression of one or more diabetes-mediating proteins. Determination of the effect of a compound may be conducted by a variety of methods known to the art, including hybridization to probes or other oligonucleotides, antibody recognition, e.g., immunodiffusion, immunofluorescence, ELISA (Enzyme-Linked Immunosorbent Assay), RIA (radioimmunoassay), blotting, immunoprecipitation, immunoelectrophoresis, or chromatography, and electrophoresis. A compound capable of increasing the expression of one or more proteins selected from the group consisting of the diabetes-mediating proteins listed in Tables 1 and 2 and decreasing the expression of one or more proteins selected from the list consisting of the diabetes-mediating proteins listed in Tables 1 and 2 is a candidate therapeutic agent for the prevention or treatment of diabetes. Changes in protein expression are determined relative to expression in the absence of the test compound.--

Please replace the paragraph starting at page 12, line 3, with the following paragraph:

--Another type of protein modification is due to the attachment of other small molecules to proteins. Examples can include, but are not limited to: (i) phosphorylation; (ii) acetylation; (iii) uridylation; (iv) adenylation; (v) methylation, and (vi) capping (diverse complex modification of the N-terminus of the protein for assorted reasons). Most of these changes are often used to regulate a protein's activity. (v) and (vi) are also used to change the half-life of the protein itself. These protein changes can be detected by 2D using several methods, such as labeling, changes in pI, antibodies or other specific techniques directed to the molecules themselves, as known in the art. Molecular weight changes can be, but may not usually be detected by 2DGE (2-dimensional gel electrophoresis). MALD (matrix assisted laser desorption of flight mass spectrometry) is preferred to detect and characterize these modifications.--

Please replace the paragraph starting at page 26, line 17, with the following paragraph:

--Diabetes-mediating proteins can be isolated in a variety of ways known to the art, including purification from biological material, expression from recombinant DNA (see above). Conventional method steps include extraction, precipitation, chromatography, affinity chromatography, and electrophoresis. For example, cells expressing a diabetes-mediating protein can be collected by centrifugation, or with suitable buffers, lysed, and the protein isolated by column chromatography, for example, on DEAE-cellulose (diethylaminoethylcellulose), phosphocellulose, polyribocytidylic acid-agarose,

hydroxyapatite or by electrophoresis or immunoprecipitation. Diabetes-mediating proteins may alternatively be isolated by immunoprecipitation with the use of specific antibodies.--

Please replace the paragraph starting at page 28, line 31, with the following paragraph:

--The development of diabetes may be monitored throughout the developmental period by determining the expression of one or more diabetes-mediating proteins and comparing ~~by comparing~~ the time of disease onset with expression and timing in the absence of disease development. Determining the expression of one or more diabetes-mediating proteins includes the diabetes-mediating protein itself, a post-translational modification product, and/or diabetes-mediating protein degradation product. In one embodiment, activation of a diabetes-mediating protein is determined by measuring the level of the diabetes-mediating protein expression in a test sample. A suitable test sample includes a body fluid, such as blood, urine, or cerebrospinal fluid, or fluid derived from it, such as plasma or serum. In a specific embodiment, the level of protein expression in a test sample is measured by Western blot analysis. The proteins present in a sample are fractionated by gel electrophoresis, transferred to a membrane, and probed with labeled antibodies specific for the protein(s). In another specific embodiment, the level of diabetes-mediating protein expression is measured by Northern blot analysis. Polyadenylated [poly(A)+] mRNA is isolated from a test sample. The mRNA is fractionated by electrophoresis and transferred to a membrane. The membrane is probed with labeled cDNA. In another embodiment, protein expression is measured by quantitative PCR applied to expressed mRNA.--